Citation:

Koutros S, Cross AJ, Sandler DP, Hoppin JA, Ma X, Zheng T, Alavanja MCR, Sinha R. Meat and meat mutagens and risk of prostate cancer in the agricultural health study. *Cancer Epidemiol Biomarkers Prev* 2008;17:80-87.

PubMed ID: 18199713

Study Design:

Prospective cohort design

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

The purpose of this study was to investigate the association between meat types, cooking methods, doneness and mutagens on the risk of prostate cancer.

Inclusion Criteria:

Participants of the Agricultural Health Study were included in this study.

Exclusion Criteria:

Exclusion criteria included the following participants:

- those who did not provide information on meat cooking practices (N=31,462);
- those with prevalent cancer cases (N=1,424); and
- females (N=1,345).

Description of Study Protocol:

Recruitment

Participants were licensed pesticide applicators recruited from the Agricultural Health Study between December 1993 and December 1997 (phase I of the study).

Design

Upon enrollment, applicators completed an enrollment questionnaire and self-administered take-home questionnaire, which inquired about dietary habits, such as supplemental vitamin intake, meat intake, cooking of meat, doneness of meat and cooking methods used for meat.

Statistical Analysis

Cox proportional hazards regression was used to estimate relative risks (RR) and 95% confidence intervals (CI). All analyses were done on three different groups: (a) all incident cases occurring after enrollment, (b) incident cases diagnosed after 1 year of follow-up, referred to as incident cases, and (c) advanced prostate cancer cases, defined as though with stage III or stage IV disease. All *p* values are two-sided. SAS statistical software was used for all analyses.

Data Collection Summary:

Timing of Measurements

Potential participants who completed an enrollment questionnaire were given a self-administered take-home questionnaire. The dietary module in the Phase I take-home questionnaire included questions on supplemental vitamin intake, meat intake, meat cooking practices (doneness and methods). A database was developed to estimate daily intake of meat mutagens based on the responses from the cooking practices module.

Dependent Variables

- Daily intake of meat mutagens: Analyzed using a specifically developed database using responses from cooking practices module (estimate intake of the following heterocyclic amines: 2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (PhIP), 2-amino-3,4,8-trimethylimidazo-[4,5-*f*]quinoxaline (DiMeIQx) and polycyclic aromatic hydrocarbons (PAH))
- Mutagenic activity in meat: determined using the standard plate incorporation assay with *Salmonella typhimurium* strain TA98, measured with revertant colonies

Description of Actual Data Sample:

Initial N: N=57,311 (all males)

Attrition (final N): N=23,080

Age: Not described

Ethnicity: Not described

Other relevant demographics: All participants were licensed pesticide applicators in Iowa or North Carolina

Anthropometrics: Not described

Location: Iowa and North Carolina

Summary of Results:

Key Findings

- During the follow-up, 668 incident prostate cancer cases were observed (613 were

diagnosed after the first year of follow-up and 140 of these were advanced cases in stage III or IV)

- Men who consumed the most red meat tended to be younger and more likely to be White, obese, have a family history of prostate cancer, be a current smoker and consume alcohol more frequently, as compared to men who had the lowest intake of red meat
- Additionally, those who consumed the most red meat tended to be less educated and less likely to take aspirin or vitamin E supplements
- Significant positive associations were found for well and very well done total meat intake and risk of prostate cancer in all case groups examined
- Suggestive evidence was found that two heterocyclic amines, DiMeIQx and MeIQx, also elevated the risk of prostate cancer among all cases, especially those with incident disease

Author Conclusion:

The authors suggested that well done meat intake may contribute to an increased risk for prostate cancer and that, although less clear, heterocyclic amine exposure may alter prostate cancer risk. The authors concluded that more research is needed to determine certainty of red meat intake on prostate cancer risk.

Reviewer Comments:

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes

2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	No
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	N/A

5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	No
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	Yes
6.6.	Were extra or unplanned treatments described?	Yes
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes

7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	Yes
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes